



Handling Clinical Trials

Applies to: [PLOS Global Public Health](#) | [PLOS One](#)

Definition

PLOS follows the [World Health Organization's \(WHO\) definition](#) of a clinical trial:

A clinical trial is any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes [...] Interventions include but are not restricted to drugs, cells and other biological products, surgical procedures, radiologic procedures, devices, behavioural treatments, process-of-care changes, preventive care, etc.

PLOS staff ensure clinical trials are labeled before you are invited to handle them. If you believe the manuscript has been misclassified, please [contact](#) the journal.

Requirements

Manuscripts describing clinical trials are monitored throughout the review process and are subjected to increased scrutiny relative to other submission types. Both you and staff editors reserve the right to reject without review any manuscripts that do not meet the following requirements.

- **Clinical trials must be registered** in a [WHO](#) or [ICMJE](#)-approved registry. Trials should be registered prospectively or must provide a clear explanation for any trials that are not prospectively registered.
- **Authors must include a copy of their IRB-approved trial protocol.** During your evaluation, compare this protocol to the methods and results reported in the manuscript to confirm that the researchers adhered to the IRB-approved procedure. Any deviations from the original protocol should be explained in the manuscript and the registry.

- **Authors must submit a completed checklist**, either [CONSORT](#) or [TREND](#), if the study was a non-randomized controlled trial as part of the Supporting Information. A CONSORT participant flowchart must be included as Figure 1 of their manuscript.

Statistical Review

Journal staff will invite a statistical reviewer to assess all clinical trial manuscripts. PLOS has a Statistical Advisory Board composed of experts in a variety of areas who work to ensure that the statistical analysis underlying all reported clinical trial results was conducted rigorously.

In addition to the statistical review, we strongly suggest that you secure at least **two reviews from subject area experts** if you decide to send the manuscript out for peer review. You may also reject the submission without review if the manuscript contains fundamental flaws. You must justify your reasoning in your decision letter.

Role of Statistical Reviewers

Statistical reviewers are asked to focus on improving study reporting and specifically, the rigor of the statistical analysis.

Specific Points We Ask Statistical Reviewers to Note

- Is there a clear statement of the objective, source of participants, and interventions being compared?
- Are randomization procedures fully detailed? Was the randomization likely to be robust and was concealment of allocation adequate?
- Was blinding (of patients, physicians, and outcome assessors) used? If not, do the authors acknowledge possible biases resulting from a lack of blinding?
- Is the study sample size properly justified (preferably with a pre-study power calculation)?
- Does the paper report on final outcomes for the full study population, and were outcomes and analyses pre-specified?

- For trials, check the manuscript against the trial registry record and/or the study protocol document (available as supporting information) and ensure any discrepancies are explained in the paper. If you are concerned about selective reporting, comment on this in your report. We recommend taking great care with reports that describe interim analyses or seem not to report on all primary and secondary outcomes.
- Is the reporting of the study population adequate? Reasons for dropout and the CONSORT flow diagram should be fully completed.
- Is reporting of harms (adverse events/side effects) adequate and balanced?
- Do the main analyses use appropriate statistical tests and are the statistical procedures referenced or described?
- Is the correct analytical population used and do the main conclusions rest on this analysis? In most cases (particularly effectiveness trials), this will be intention-to-treat, not per-protocol.
- Are the main statistical results given using estimates of effect size and an indication of precision (uncertainty, typically 95% confidence intervals)?
- Most guidance discourages reliance on p-values, which do not enable readers to distinguish between "negative" and "inconclusive" results nor to draw clinically relevant interpretations from the observed difference between groups.
- In general is statistical material presented adequately (figures, tables etc.)? Is there appropriate correction for multiple testing? Reports should use exact p-values not notation such as stars, N.S., non-significant, etc.
- Papers should report absolute as well as relative risks, or use numbers needed to treat.
- Do authors discuss results in a balanced way (without "spin")? Be sure to evaluate this in the abstract, not just the full paper. Potential biases should be properly discussed by authors.



Additional Points

We also ask the reviewers to read our guidelines for reviewers ([One](#) | [GPH](#)) online to familiarize themselves with the scope, purpose, and editorial criteria of the journal.

The journals are particularly focused on methodological rigor and quality of reporting. We do not consider the direction of results (i.e., whether "positive" or "negative") to be relevant to editorial decisions, providing the study is adequately powered, well conducted, and clearly reported. We ask reviewers to therefore disregard the direction of findings in their evaluations and submitted reports. We are therefore looking for a detailed review covering all aspects of quality of design, statistical analysis, and reporting of the study.

The journal supports widely endorsed community standards for trial conduct and reporting, such as the [CONSORT guidelines](#) for registered clinical trials. The statistical reviewers are encouraged to refer to the study protocol supplied by the authors and to consider issues of reporting bias when evaluating the validity of the published paper. We ask reviewers to ensure they highlight any protocol deviations and whether these seem to be important or not when providing their report to the journal.

Links to more Resources for Editors

[PLOS Global Public Health](#) | [PLOS One](#)

Need help? Contact

globalpubhealth@plos.org | plosone@plos.org

edboardsupport@plos.org